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Cheating, or an Early Mingling of the Blood?

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Last month, when the champion American cyclist Tyler Hamilton was accused of blood doping, or transfusing himself with another person's blood to increase his oxygen-carrying red cells, he offered a surprising defense: the small amount of different blood found mixed in with his own must have come from a "vanishing twin."

In other words, his scientific expert argued, Mr. Hamilton had a twin that died in utero but, before dying, contributed some blood cells to him during fetal life. And those cells remained in his body, producing blood that matched the dead twin and not Mr. Hamilton. Or perhaps it was his mother's blood that got mixed in during fetal life.

An arbitration panel did not believe those hypotheses and said there was a "negligible probability" that Mr. Hamilton was anything but guilty.

The test, they concluded in a 2-to-1 decision, shows a blood transfusion and that meant that Mr. Hamilton was suspended from racing for two years, the first and only person convicted for that offense. At age 34, near the end of his career, it could mean his championship days are over.

Mr. Hamilton has said he will appeal the decision. If he can prove the test was flawed, then not only might he return to cycling and his multimillion-dollar career, but other athletes could use the same defense. The new test, developed over two years by the World Anti-Doping Agency and the United States Anti-Doping Agency, would be all but useless.

Travis T. Tygart, the general counsel for the United States Anti-Doping Agency, which prosecuted Mr. Hamilton, says the scientific evidence was against the cyclist.

"Our interest is only justice," Mr. Tygart said. "We don't blindly bring doping cases. We look at the evidence, and if we think there is enough evidence to go forward we present that to an arbitration panel."

Whether Mr. Hamilton is guilty or innocent, his defense does refer to a real phenomenon. Researchers who have no involvement in Mr. Hamilton's case say it actually is possible for someone to have two types of blood in his body, without doping. They emphasize that they do not know whether this is the case with Mr. Hamilton.

One route to this odd state, called chimerism, is the vanishing twin. Dr. Helain Landy of Georgetown University, who has no involvement in the Hamilton case, has found that 20 to 30 percent of pregnancies that start out as twins end up as single babies, with one twin being absorbed by the mother during the first trimester.

Others researchers have found that in some cases, before the twin is absorbed, some of its cells enter the body of the other fetus and remain there for life. The cells can include bone marrow stem cells, the progenitors of blood cells.

Another route to chimerism is through the cells that routinely pass from a mother to fetus and remain there for life.

Dr. Ann Reed, chairwoman of rheumatology research at the Mayo Clinic, who uses sensitive DNA tests to look for chimerism, finds that about 50 to 70 percent of healthy people are chimeras. The more scientists look for chimerism, the more they find it. It seemed not to exist in the past, she said, because no one was explicitly looking for small amounts of foreign cells in people's bodies.

"Some believe that if you look hard enough you can find chimerism in anybody," said Dr. Reed, who also has not been involved in the Hamilton case. It is so common that she thinks there must be a biological reason for it. It also may cause problems, she and others say.

Chimerism may be why bone marrow from a seemingly perfectly matched donor relentlessly attacks a patient who receives it in a transplant - the attackers may be a small percentage of cells in the marrow that come from someone else. It also may help explain autoimmune diseases, when the body's own immune cells attack. The attacking cells may be the foreign ones that arise from someone

else.

The Hamilton case involves a test developed by Dr. Margaret Nelson and her colleagues at the Royal Prince Alfred Hospital in Australia. It was based on a simple idea: if an athlete got a transfusion, he would have to make sure the blood was the right match using the blood antigens A, B and O. But blood cells have other surface proteins, so-called minor antigens, that do not matter in blood typing for transfusions but can be used to distinguish one person's blood from another's. The investigators said they could use a sensitive test, flow cytometry, to search for small amounts of blood with minor antigens different from those in the athlete's own blood.

It was an important advance, anti-doping agency officials said. They knew that athletes, including cyclists, had used blood transfusions in the past to boost their performance but had no test to prove it.

The principal hematologist working with the anti-doping agencies, Dr. Ross Brown of Royal Prince Alfred Hospital, rejects the idea that the test could be finding chimeras instead of transfusions. In his testimony at Mr. Hamilton's hearing and in an e-mail message Dr. Brown, who is Dr. Nelson's immediate supervisor, said chimerism was so rare as to be inconceivable as an explanation for Mr. Hamilton's results. "The only reasonable explanation is a transfusion," he wrote by e-mail.

Dr. Brown, the only outside scientist that the anti-doping agency suggested to present its point of view, said that blood banks almost never found chimeras. The blood banks used a less sensitive test, but Dr. Brown testified that he himself, using the more sensitive flow cytometry on at least 20,000 blood samples, never found a chimera.

And, he said, reports of people with small amounts of foreign cells do not signify that an athlete with a second population of blood cells had someone else's blood stem cells in his bone marrow. Moreover, he said, Mr. Hamilton tested negative a few months after his positive test last fall. That is consistent with an athlete who had transfusions, was caught, and then stopped.

In addition, Dr. Brown said, another rider on Mr. Hamilton's team, Santiago Perez, also tested positive. (He did not show up for his hearing and was pronounced guilty in absentia.)

"It seems inconceivable to me that there would be two people who were rare chimeras on the same cycling team," Dr. Brown wrote by e-mail.

Dr. Olivier Rabin, the scientific director of the World Anti-Doping Agency, said the onus was on Mr. Hamilton to prove he was innocent. "It is up to the defending party to prove it is anything other than blood doping," he said.

The story of Mr. Hamilton's scientific defense began last September, when the blood doping allegations were first made public. He had just won a gold medal in the Athens Olympics and had competed in a bicycle race in Spain when the World Anti-Doping Agency said his blood revealed transfusions.

"I was so calm," Mr. Hamilton recalled, thinking the result was a mistake. "I knew something was wrong and we would get to the bottom of it."

The next morning, Dr. David Housman, a molecular biology professor at the Massachusetts Institute of Technology and an avid Red Sox fan, was reading the sports pages for baseball news and came across an article on Mr. Hamilton.

Dr. Housman, who never took much interest in bicycle racing, was jolted by what he read.

"I read it and said: 'Wait a second. I don't think the explanation they give for the blood test is the only possible explanation,'" he said.

He knew the science showing that chimeras are not so unusual. And he knew that stem cells turn off and on throughout life so that a stem cell from a twin, for example, might be producing red blood cells and then stop, making a tiny amount of foreign blood come and go at random.

So Dr. Housman looked up Mr. Hamilton's father, Bill, on the Internet and wrote him a letter offering to help, for no fee.

Bill Hamilton was astonished.

"We were so grateful," he said. "At the time, we didn't know which way to turn, and then out of the blue came this brilliant scientist from M.I.T. wanting to help."

Not only was a vanishing twin or chimerism a real possibility, Dr. Housman decided, but he had real questions about whether the test was reliable enough to use to look for blood doping.

Dr. S. Gerald Sandler, a professor of medicine and pathology at Georgetown University Hospital, who previously was medical director for the national reference laboratory for blood group serology at the National Red Cross and who has no involvement in the Hamilton case, said the test was acceptable for research. But, he said, its results could easily differ from lab to lab. It "is being misapplied," he said, when it is used to accuse athletes of blood doping.

Dr. V. K. Gadi, a hematologic oncologist at the Fred Hutchinson Cancer Center in Seattle, who uses flow cytometry in his research, says that "the test can be quite finicky from experiment to experiment," and that the results can vary depending on how the experimenter sets up the test.

But the two arbitrators who ruled against Mr. Hamilton said they were confident that the test was accurate. Although, they wrote, "There are no scientific studies that detect false positives in the use of the HBTT," referring to the test, "there is no need to do so because there is no suggestion in the use of the HBTT that it produces false positives."

Mr. Hamilton hopes to be vindicated on appeal. In the meantime, preparing to race again, he is training in Boulder, Colo. After riding for four to seven hours a day he e-mails his training files to a coach in Italy who oversees his program.

Bicycling, his wife, Haven, said, is his life. "He still loves it," she said.